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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/120,970	07/22/1998	ROY CURTISS III	53116-1763	2800

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 06/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/120,970	**Applicant(s)** CURTISS ET AL.	
	Examiner Ginny Portner	**Art Unit** 1645	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 14 April 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *14 April 2006*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: none.
   Claim(s) objected to: *35*.
   Claim(s) rejected: *30,32-39,41-51,53-65*.
   Claim(s) withdrawn from consideration: none.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☒ Other: See attached

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TECHNOLOGY CENTER 1600

Continuation of 3. NOTE: new claim 66 was not finally rejected, and the scope of claim 66 is broader than finally rejected claim 39 for which claim 66 is suppost to be a replacement, in light of the cancelation of claim 35.

Continuation of 11. does NOT place the application in condition for allowance because: the correspondence table compared the instant method with a composition claim, rather than the method claim of the issued patent utilized in the obviousness type double patenting rejection made of record; additoinally new claim 66 is of broader scope than prior claim 35 which raises new issues after final..

Correspondence table between the instant Application claims 09/120,970 (claims 30, 32-33, 35-60 and 65) and allowed methods claim 24, in light of the compositions defined in claims 1-23 of US Pat. 6,780,405.

The disclosure of 6,780,405 is utilized for definitions of the claimed method, the method administering the allowed compositions defined therein.

The environmentally regulateable control sequence is a coding sequence effected by environmental arabinose.

09/120,970	**6,780,405**
* **method** **claim** 30	*claim 24 (dep. From clm 1,5,19)
* **inducing**	***inducing**
immune	**immunoprotection**
response	**(species of immune response)**
***administering**	* **administering**
* **attenuated bacterial cell/**(instant claim 30, 36, 37)	* **inactivated Salmonella** (clm. 6, 8)
expression gene	**encodes desired gene product**
***antigen introduced into the animal**	***antigen admin. (introduced) to vertebrate**
***containment system (viable in animal/nonviable outside)**	***RADS is a species of containment system**

'405 at col. 23, lines 21-38 and col. 24, lines 32-35 defines the RADS to comprise ELVS components and '405, allowed claims 21-22 are so defined:

- "In that system, vector-borne lethal genes such as the phage lysis genes lys 13 and lys 19 are operably linked to P22 P.sub.R and the chromosome-encoded C2 repressor is operably linked to **araCP.sub.BAD** (claimed in '405, allowed claims 7, 10, 12 which depend from claim 5). **Introduction of the strain into an environment without arabinose, such as in an inoculated**

animal, results in a dilution of the C2 repressor present until the lethyl gene products kill the cell. In addition, the RADS with a RAV comprising a transfer vector can be designed as an ELVS that lysis due to regulated lysis genes inserted into the chromosome. Such expression of lysis genes would exhibit delayed expression such that lysis would only occur after the vertebrate cells with the transfer vector had entered a eukaryotic cell and conferred runaway vector replication. See also Example 6, which describes novel transfer vector adaptations to the RADS. When properly designed, the ELVS system is fully compatible with the RADS system and may share control elements. In this case, lysis of the cell, for example caused by an ELVS, will release the transfer vector inside the recipient cell."

Additionally, the '405 Specification definitions set forth the AraCPbad regulatory control sequence to be an integral component of a RADS containment system, this regulatory control being claimed in '405 allowed (claims 5-7 and 21- 22).

- "Depending on the turnover of the trans regulatory element and the relationship between the amount of trans regulatory element on hand and the amount of trans regulatory element needed to maintain the low copy number regime, the low copy number regime can be maintained for several generations after transfer to the high copy number environment. Such temporary low copy number condition can be useful, for example, for allowing the host microorganism to colonize the host in a high copy number environment (e.g., without arabinose), such as an animal, but not remain indefinitely. As such, the **RADS is a containment system** even without the phage lysis genes described in WO96/40947. A delayed RADS is also useful when the desired gene product is harmful to the host cell, as in Example 3. Additionally, the delayed RADS can be used to depend **an essential gene of a balanced lethal host**

system, such as asd, on an activateable control sequence such as araCP.sub.BAD, to provide for a weakening of the cell wall upon immunization (and withdrawal of, in this case, arabinose). See Example 5." The "araCPsubBAD" control sequence is claimed in '405 claim 7 which depends from claim 5, form which the method claim 24 indirectly depends.

Clm 32: antigen sources	claim 24 : antigen, defined to be a vaccine antigen Col. 31, lines 30-35
Clm 33: mucosal	claim 24: admin. MALT (mucosal: column 13,lines 24-29;col. 31,lines 24-25)
Clm. 35: replication gene	"a second ori conferring vector replication " Allowed claim 1.
Clm. 38: GALT or BALT	claim 24: admin. GALT or BALT ('405, col.13, lines 14-19)
Clm 39: lethal gene	claim 24: "lethyl gene product kills the cell",col. 23,lines 25-26
Clm. 40-43: cell wall essential gene	Clm. 24: balanced lethal system, asd gene is an essential gene for cell wall biosynthesis (see examples and col. 23-24).
Clm. 45-46: P22 lysis genes 13 & 19	Clm 24: defined microorganism to include the P22 lysis genes, 13 & 19; also see allowed claims 18-23; col. 23, lines 21-38 and col. 24, lines 32-35 defines the RADS to comprise ELVS, the lysis genes being integrated into the bacterial chromosome and are not located on the plasmid runaway vector.

- Therefore, the corresponding support for each of the recited claim limitations shows the allowed method claim 24 of '405 to be defined as a species within the claimed genus of methods of the instant Application.
- The allowed species still anticipates the instantly claimed genus of methods.
- The obviousness type double patenting could be obviated by submission of an effective terminal disclaimer.

1. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on flextime, but usually M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Vgp
June 1, 2006

DETAILED ACTION

Claims 30,32-33,35-39,41-51,53-65 are pending.

Objections/Rejections Withdrawn

1. (Claim Objections Withdrawn)Claims 35, 52 and 65 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim has been obviated through amendment or cancellation of claims.
2. Claims 43,44-45,47,51,53-55 and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reciting abbreviations that do not clearly define the claimed invention as the meaning of the abbreviations is not structurally, nor functionally defined in the claims, in light of the amendment of the claims and remarks clarifying the terms of the claims.
3. Claim 30, 32-33,35-38, 39, 50-60 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over US Pat.5,294,441; 5,387,744; 5855,879 and 5,855,880 are herein withdrawn in light of Applicant's remarks and the recombinant bacteria requiring the essential gene that is not chromosomally associated to be under the control of an environmentally regulate-able control sequence.
4. (35 U.S.C. 112, second paragraph, Rejection Withdrawn) Claims 30 and 65 rejected under, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention have been obviated in light of the claim amendments to provide for antecedent basis for the term chromosomal copy and amendment of claim 65 to depend from claim 30.

Objections/Rejections Maintained

5. (Claim Objection Maintained) Claims 35 objected to for minor informalities, specifically claim 35 is still objected to for depending from a later number claim 39, in light of the fact that claim 35 still depends from claim 39.

6. (Claim Rejections - 35 USC § 112 Maintained) The rejection of Claims 61-64 under 35 U.S.C. ə 112, first paragraph as failing to provide an enabling disclosure in light of the fact that the extra chromosomal vector comprising pMEG-104 is required to practice the claimed invention and not so described, known and readily available to the public or obtainable by a repeatable method set forth in the specification was not addressed and therefore maintained for reasons of record.
7. Claim 30, 32-33,35-38, 39-60, 65 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over US Pat 6,780,405 is maintained for reasons of record and responses set forth below to Applicant's remarks.

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claim 30, 32-33,35-38, 39, 50-60 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 24 and claims 1-23 (claim 20 defined to include Salmonella) of U.S. Patent No. **6,780,405**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the allowed species of method of inducing an immunoprotective immune response in a vertebrate anticipates the instantly claimed invention of inducing any type of immune response in an animal, wherein the composition administered in the instant Application comprises a bacteria that may or may not be attenuated, but the allowed species of microorganism must be attenuated (see claim 19), the viability system of the instant Application may be controlled by any number or regulate able control sequences, but the allowed method administers a species which requires specific regulatory sequences (see claims 1-18).

7. Claim 30, 32-33,36-37, 41-43 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 4, 12 defined to include Salmonella strains of claims 59 of U.S. Patent No. **5,294,441**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the allowed species of method of stimulating an immune response in an individual anticipates the instantly claimed invention of inducing any type of immune response in an animal, wherein the composition administered in the instant Application comprises a bacteria that may or may not be attenuated,